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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,322	04/23/2001	Long Y. Chiang	06897-006001	4062

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,322	CHIANG, LONG Y.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Reciept of amendment and remarks dated 3-25-05 and power of attorney dated 5-31-05 is acknowledged.

Claims 1-21 are pending in the instant application.

Response to Arguments

Applicant's arguments filed 3-25-05 have been fully considered but they are not persuasive.

1. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting the growth of tumor cells in a tumor site by administering sulfobutylated hexadecaniline, does not reasonably provide enablement for all the oligoaniline derivatives that are within the scope of claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

RESPONSE: Applicants argue that the oligoanilines recited in claim 1 contain at least one hydrophilic group and possess two common structural features: (1) capability of generating free radicals upon irradiation (due to the presence of electron-rich oligoaniline moieties) and (2) enhanced water-solubility (due to the presence of hydrophilic groups), and thus high bioavailability. It is argued that to practice the method of claim 1, one first delivers an oligoaniline of formula (1) to a tumor site only and then irradiates the site to generate free radicals, which further convert surrounding molecular

oxygen to highly reactive oxygen radicals, which in turn attack and damage tumor cells, thereby inhibiting their growth. While applicants agree that the oligoanilines covered by formula (1) recited in claim 1 are different from each other, they argue that the compounds share the two above-mentioned common structural features and, due to the two structural features, they all can exert inhibition activity on tumor growth.

Applicants' arguments are not found persuasive because instant compound of formula I encompasses multitudes of compound that possess oligoaniline moiety. The variables X, W and K include groups that are not necessarily hydrophilic. In particular, W includes ester or ether or thioether groups; K includes amine and amide containing moieties. Thus, the claimed compounds still encompass non-hydrophilic compounds that do not necessarily possess the argued structural features required for practicing the claimed method.

With respect to the undue experimentation, applicants argue that it is a mere routine procedure to determine the degrees of therapeutic efficacy among different oligoanilines having the two common structural features. Further, it is argued that, enablement of claim 1 does not require testing the efficacy of each oligoaniline of formula (1) recited therein. It is argued that applicants are not required to disclose every species encompassed by their claims even in an unpredictable enablement of claim 1 also does not require testing the efficacy of an oligoaniline in all types of tumors. Applicants' arguments are not persuasive because as explained above, the claimed composition includes numerous compounds that do not necessarily possess the above features owing to the non-hydrophilic groups. Therefore, one of skilled in the art would

not be able to predict the efficacy of the compounds for inhibiting the growth of tumor cells without undue experimentation.

Applicants argue a skilled person would readily understand the rationale in view of the specification and common knowledge in the art because the oligoaniline covered by formula (1) recited in claim 1 is delivered to a tumor site only and that it is well known that tumor tissues differ substantially from normal tissues, it would not generate free radicals in the absence of irradiation. In particular, it is argued that example 4 in the Specification describes that the average tumor weight of the mice treated with an oligoaniline of formula (1) was about 40% (a 60% reduction) of the average tumor weight of the untreated mice. However, the arguments are not persuasive because once again it is emphasized that not all the compounds encompassed by instant claimed compound I include not only hydrophilic but hydrophobic moieties that not possess the capability of generating free radicals, that is essential for practicing the instant invention. With respect to the example cited, the claimed effect is limited to the specific compound (hexadecaniline) but not any and all the compounds covered by claimed compound I because the compound exemplified is not representative of the compound I. Thus, a skilled artisan would have to test the compounds covered by compound I for their efficacy in generating free radicals and reducing tumor size. Therefore, for the above reasons instant rejection has been maintained.

2. Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al (Macromolecules 1994, submitted on IDS).

Nguyen et al teach polyaniline polymers that have high electrical conductivity and are highly water-soluble. The monomers that make up oligoaniline polymers are described in col. 2 of page 3625. Particularly, compounds of formula III read on the claimed compounds (sulfobutylated aniline polymers). On page 3626, col. 1, Nguyen teaches preparing the soluble aniline polymers not just in water, but in dispersants, which meet the claimed carrier. Instant claims recite m=2-6. While Nguyen et al does not specifically teach the length of the polymer, the number of aniline monomer in the teachings of Nguyen range form 1 to 4 9formula in col. 2, page 3625). Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to prepare sulfonylated aniline polymers having a desired chain by routine optimization, without loosing the electrical conductivity and water solubility of the compounds.

RESPONSE: Applicants state that Claim 18 covers a pharmaceutical composition containing an oligoaniline of formula (1) and a pharmaceutically acceptable carrier. Applicants argue that Nguyen discloses synthesis and properties of certain water-soluble conducting polyaniline copolymers but does not disclose or suggest a pharmaceutical composition containing both a polyaniline copolymer and a pharmaceutically acceptable carrier, as required by claim 18. Applicants argue that Nguyen describes physical properties (e.g., conductivities and color changes) of certain water-soluble conducting polyaniline copolymers but nowhere in Nguyen is a

composition containing a polyaniline polymer and a pharmaceutically acceptable carrier disclosed or even suggested. It is argued that the pharmaceutical compositions of claim 18 are developed based on the following facts: (1) blood vessels in tumor tissues are much more permeable to plasma than those in normal tissues, (2) cell growth can be inhibited by free radicals, (3) the oligoanilines used in the compositions of claim 18 are capable of generating free radicals upon irradiation, and (4) these oligoanilines possess enhanced bioavailability and are suitable for use in a pharmaceutical composition. Finally, it is argued that Nguyen does not disclose or suggest any of these facts and thus one skilled in the art, in view of Nguyen, would not have been motivated to use polyanilines in the pharmaceutical compositions of claim 18. Applicants' arguments are not persuasive because instant claim is directed to a composition and not a method. Nguyen states, "It should be mentioned that, besides modifying the polyaniline polymers to make them inherently soluble in aqueous solutions, polyaniline has also been solubilized by combining it with dispersants", thus making it clear that an aqueous solution of the compound is prepared, which reads on the composition because water meets the claimed carrier limitation. Further, the claim limitation "for inhibiting the growth of tumor cells" is an intended use but not a positive limitation and accordingly the argument that the reference does not disclose a pharmaceutical carrier for the claimed effect is not persuasive.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -6.30 PM

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lakshmi S Channavajjala
Examiner
Art Unit 1615
June 8, 2005

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